REMARKS

Claims 1-22 are pending in the application. Claims 1-11, 13-18 and 20-22 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to non-elected invention. Claims 12 and 19 are amended. Claims 23-27 are added. Support for the amended and newly added claims can be found throughout the specification of the original PCT application (especially page 33), and the translation thereof including the corrected portion of page 29 of the specification discussed below.

The applicants amended the paragraphs on page 29, line 26 to page 30, line 12 in the specification in order to accurately reflect the original Japanese text of PCT Application No. PCT/JP02/13640. The scope of the corrected translation of the present application does not exceed the scope of the originally filed international application in Japanese. The verification, clean copy and marked up copy of relevant part of the specification are attached hereto.

No new matter has been introduced by the instant amendments. Applicants reserve the right to pursue the subject matter cancelled by this or a prior action in this or a subsequent continuation application.

Claims 12 and 19 stand rejected under 35 U.S.C. 102(e) as being anticipated by Jenuwein et al. (US PAT 6689583) and Jenuwein et al. (US PAT 6555329).

Claims 12 and 19 stand rejected under 35 U.S.C.§112, first and second paragraphs.

Rejection under 35 USC § 112

Claims 12 and 19 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. The examiner stated that the claims recite

methods of using a protein to screen for cancer preventive/therapeutic agents or apoptosis inducers but do not define **how** the protein is used. What action comprise the claimed methods.

The rejection is respectfully traversed.

The amended claims are directed to methods of screening a preventive or therapeutic agent for cancer, and an apoptosis inducer, respectively. The method comprises measuring and comparing the radioactivities of histone H3 or a polypeptide having the N-terminal sequence of histone H3 by transfer of the methyl group, (i) in the case where a protein containing the amino acid sequence of SEQ ID NO: 1 or a salt thereof is reacted with (a) S-adenosyl-L-methionine wherein the methyl group is radio-labeled and (b) histone protein or a polypeptide having the N-terminal sequence of histone H3 and (ii) in the case where a protein containing the amino acid sequence of SEQ ID NO: 1 or a salt thereof is reacted with (a) S-adenosyl-L-methionine wherein the methyl group is radio-labeled and (b) histone protein or a polypeptide having the N-terminal sequence of histone H3 in the presence of a test compound.

How the protein is used is clearly defined in the claims. Namely, the protein is used by being reacted with (i) (a) S-adenosyl-L-methionine wherein the methyl group is radio-labeled and (b) histone protein or a polypeptide having the N-terminal sequence of histone H3, or (ii) (a) and (b) and a test compound. Then the activity of the protein is measured as radioactivity and the level of the radioactivity are compared.

Claims 12 and 19 stand rejected under U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor at the time the application was filed, had possession of the claimed invention. The Office Action stated that the specification does not contain any disclosure of the methods of identifying preventive/therapeutic agents for cancer or apoptosis inducer using all functionally different proteins that are substantially the same amino acid sequence (50% to 95% identity to) to SEQ ID NO: 2 or fragments thereof.

The rejection is respectfully traversed.

As stated above, the amended claims are directed to methods of identifying preventive/therapeutic agents for cancer or apoptosis inducer using a protein containing the amino acid sequence of SEQ ID NO: 1 or a salt thereof. As the examiner admitted, the specification discloses use of the amino acid sequence of SEQ ID NO: 1 or a salt thereof. Therefore, one skilled in the art can reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 12 and 19 stand rejected under 35 U.S.C. 112, first paragraph. The Office Action stated that claims 12 and 19 are so broad as to encompass methods for identifying inhibiting agents for proteins that are substantially the same amino acid sequence (50% to 95% identity to) to SEQ ID NO: 1 or fragments thereof and then identifying the agents to use as preventive/ therapeutic agent for any cancer or apoptiosis inducer, thus not reasonably provide enablement.

The rejection is respectfully traversed.

As the Examiner admitted, the specification is "enabling for identifying inhibiting agents for histone methyl transferase of SEQ ID NO: 1 and then identifying the agents to use as a therapeutic agent for a specific cancer." The amended claims 12 and 19 are directed to methods of identifying preventive/therapeutic agents for cancer or apoptosis inducer using a protein containing the amino acid sequence of SEQ ID NO: 1 or a salt thereof. Thus, the scope of the claims is commensurate with the enablement provided by the disclosure with regard to the protein used by the methods of the claims.

Accordingly, applicants have provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims

Rejection under 35 USC § 102(e)

Claims 12 and 19 stand rejected under 35 U.S.C. 102(e) as being anticipated by Jenuwein et al. (US PAT 6689583).

The rejection is respectfully traversed.

The amended claims 12 and 19 are directed to methods of screening for a preventive or therapeutic agent for cancer, and an apoptosis inducer, respectively. The method comprises measuring and comparing the radioactivities of histone H3 or polypeptide having the N-terminal sequence of histone H3 by transfer of the methyl group, (i) in the case where a protein containing the amino acid sequence of SEQ ID NO: 1 or a salt thereof is reacted with (a) S-adenosyl-L-methionine wherein the methyl group is radio-labeled and (b) histone protein or a polypeptide having the N-terminal sequence of histone H3 and (ii) in the case where a protein containing the amino acid sequence of SEQ ID NO: 1 or a salt thereof is reacted with (a) S-adenosyl-L-methionine wherein the methyl group is radio-labeled and (b) histone protein or a polypeptide having the N-terminal sequence of histone H3 in the presence of a test compound.

The Office Action stated that Jenuwein et al. (US PAT 6689583) teaches methods of screening modulators of Human SUV3 protein (chromatin- regulatory protein) of SEQ ID NO: 4 which has 100% sequence identity with the SEQ ID NO: 1 of the present application and suggested their use as therapeutic agents for cancer and apoptosis inducer. However,

> "[t]he disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation."

MPEP 2121.01, cited *Elan Pharm., Inc. v. Mayo Found. For Med. Educ & Research*, 346 F3d 1051, 1054. Here, Jeuwein et al (US PAT 6689583, hereinafter the '583 patent) merely generally describes a screening method of modulators of histone methyl transferase. The '583 patent neither teaches nor even suggests all of the elements of the claimed invention recited in claims 12 and 19. Thus, the invention of the amended claims should not be anticipated by the '583 patent.

Further, Claim 12 and 19 are rejected under 35 USC 102 (e) as being anticipated by Jenuwein et al. (USP 6555329). The Office Action stated that Jenuwein et al

describes a screening method of modulators of histone methyl transferases of SEQ ID NO: 7 (having 56.1% sequence identity with SEQ ID NO:1 of the present application).

The rejection is respectfully traversed.

The amended claims 12 and 19 are directed to screening methods with use of a protein containing the amino acid sequence of SEQ ID NO: 1 or a salt thereof. Accordingly, the claims 12 and 19 are patentably distinguishable over the '329 patent.

In view of the foregoing, applicants respectfully request reconsideration, withdrawal of all grounds of rejection and objection, and allowance of claims 12, 19 and 23-27 in due course. The Examiner is invited to contact applicants' undersigned representative by telephone at the number listed below to discuss any outstanding issues.

Respectfully submitted,

Date: April 10, 2006

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VERIFICATION OF TRANSLATION

I, the undersigned Hiroshi Kobayashi, Japanese Patent Attorney, having an office at Fukuoka Building, 9th Floor, 8-7, Yaesu 2-Chome, Chuo-ku, Tokyo 104-0028 Japan, declare that I am well acquainted with the Japanese and English languages, and that the attached English text is, to the best of my knowledge, a complete and accurate translation from the Japanese text of page 33, lines 3-18 of the specification of PCT Application No. PCT/JP02/13640, which corresponds to page 29, line 26 to page 30, line 12 of the U.S. Patent Application Serial No.:10/500,216.

The undersigned further declares that all statements made herein of his/her own knowledge are true, and all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like, so made, are punishable by fine and/or imprisonment under Section 1001 of Title 18 of the United States Code, and that any such willful false statements may jeopardize the validity of the application or any patent resulting therefrom.

Date: April 7, 2006

Signature of verifying person

Hiroshi Kobayashi
Printed Name of verifying person

ストンH3のN末端配列を有するポリペプチドを接触させた後、試験化合物を添加してもよい。

また、(i')本発明のタンパク質、S-アデノシル-L-メチオニンおよびヒストンタンパク質またはヒストンH３のN末端配列を有するポリペプチドを反応させた場合と、(ii')本発明のタンパク質、S-アデノシル-L-メチオニンおよびヒストンタンパク質またはヒストンH３のN末端配列を有するポリペプチドを、試験化合物の存在下、反応させた場合の、メチル化（ジメチル／トリメチル化）リジン残基を、例えば抗HistoneH3（dimethyl/trimethyl lysine9）抗体などを用いてそれぞれ測定し、本発明のタンパク質の活性を調節（促進または阻害、好ましくは阻害）する化合物またはその塩をスクリーニングする。

また、(i')本発明のタンパク質、S-アデノシル-L-メチオニンおよびヒストンタンパク質またはヒストンH3のN末端配列を有するポリペプチドを反応させた場合と、(ii')本発明のタンパク質、S-アデノシル-L-メチオニンおよびヒストンタンパク質またはヒストンH3のN末端配列を有するポリペプチドを、試験化合物の存在下、反応させた場合の反応生成物を適宜精製し、マススペクトロメトリー（例、TOF-MSなどを用いる）を計測することにより、メチル化に伴う分子量の変化を指標に、本発明のタンパク質の活性を調節（促進または阻害、好ましくは阻害）する化合物またはその塩をスクリーニングする。

上記の本発明のタンパク質は、好ましくは、本発明のタンパク質をコードするＤＮＡを含有する形質転換体を培養することによって製造されたものである。さらには、本発明のタンパク質を発現し得る細胞を用いて同様に反応させて、メチル基転移によるヒストンH3またはポリペプチドの放射活性を測定してもよい。

本発明のタンパク質を産生する能力を有する細胞としては、例えば、前述した本発明のタンパク質をコードするＤＮＡを含有するベクターで形質転換された宿主（形質転換体）が用いられる。宿主としては、例えば、ＣＯＳ７細胞、ＣＨＯ細胞、ＨＥＫ２９３細胞などの動物細胞が好ましく用いられる。該スクリーニングには、例えば、前述の方法で培養することによって、本発明のタンパク質を発現させた形質転換体が好ましく用いられる。本発明のタンパク質を発現し得る細胞の培養方法は、前記した本発明の形質変換体の培養法と同様である。

Accurate English Translation of the description at page 33, lines 3-18 of PCT Application No. PCT/JP02/13640, which should have appeared at page 29, line 26 to page 30, line 12 of the present specification

Also, methylated (dimethylated/trimethylated) lysine residues are assayed using anti-histone H3 (dimethyl/trimethyl lysine 9) antibody, etc., respectively, (i') in the case where the protein of the present invention is reacted with S-adenosyl-L-methionine and histone protein or a polypeptide having the N-terminal sequence of histone H3 and (ii') in the case where the protein of the present invention is reacted with S-adenosyl-L-methionine and histone protein or a polypeptide having the N-terminal sequence of histone H3 in the presence of a test compound, whereby the compound or its salt that regulates (promotes or inhibits, preferably inhibits) the activities of the protein of the present invention is screened.

Furthermore, the reaction products obtained (i') in the case where the protein of the present invention is reacted with S-adenosyl-L-methionine and histone protein or a polypeptide having the N-terminal sequence of histone H3 and (ii') in the case where the protein of the present invention is reacted with S-adenosyl-L-methionine and histone protein or a polypeptide having the N-terminal sequence of histone H3 in the presence of a test compound, are appropriately purified and mass spectrometry is performed (using, e.g., TOF-MS, etc.). Thus, the compound or its salt that regulates (promotes or inhibits, preferably inhibits) the activities of the protein of the present invention is screened using as an indicator changes in molecular weight accompanied by methylation.

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Accurate English Translation of the description at page 33, lines 3-18 of PCT Application No. PCT/JP02/13640, which should have appeared at page 29, line 26 to page 30, line 12 of the present specification

Also, methylated (dimethylated/trimethylated) lysine residues are assayed using anti-histone H3 (dimethyl/trimethyl lysine 9) antibody, etc., respectively, (i') in the case where the protein of the present invention is reacted with S-adenosyl-L-methionine ~~wherein the methyl group is radio-labeled~~ and histone protein or a polypeptide having the N-terminal sequence of histone H3 and (ii') in the case where the protein of the present invention is reacted with S-adenosyl-L-methionine ~~wherein the methyl group is radio-labeled~~ and histone protein or a polypeptide having the N-terminal sequence of histone H3, in the presence of a test compound, whereby the compound or its salt that regulates (promotes or inhibits, preferably inhibits) the activities of the protein of the present invention is screened.

Furthermore, the reaction products obtained (i') in the case where the protein of the present invention is reacted with S-adenosyl-L-methionine ~~wherein the methyl group is radio-labeled~~ and histone protein or a polypeptide having the N-terminal sequence of histone H3 and (ii') in the case where the protein of the present invention is reacted with S-adenosyl-L-methionine ~~wherein the methyl group is radio-labeled~~ and histone protein or a polypeptide having the N-terminal sequence of histone H3, in the presence of a test compound, are appropriately purified and mass spectrometry is performed (using, e.g., TOF-MS, etc.). Thus, the compound or its salt that regulates (promotes or inhibits, preferably inhibits) the activities of the protein of the present invention is screened using as an indicator changes in molecular weight accompanied by methylation.